K010301

JUN 11 2001

# 510(k) Summary


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| Date: | 7 June, 2001 |


| | |
|---|---|
| Device Name | ImmunoWELL® EA(D) IgG Test |
| Common, usual, or classification name | Ant- EBV EA-D, Enzyme Immunoassay |
| Classification Name | Epstein-Barr Virus, Other |
| Classification Number (if known) | 866.3235 |

## Identification of the legally marketed device substantial equivalence is claimed:

Wampole Laboratories EA-D IgG ELISA, manufactured by Trinity Biotech. 510(k) notification is registered by Clark Laboratories, owned by Trinity Biotech.

## Description of the new device:

The ImmunoWELL Test utilizes an EIA microtiter plate technique for the detection of antibodies. Serum is added to antigen coated microtiter wells and allowed to react. After removal of unbound antibodies, horseradish peroxidase-conjugated antihuman IgG antibodies are allowed to react with bound antibodies. The bound peroxidase reacts with tetramethylbenzidine (TMB), the chromogenic substrate, developing a color. Finally, the substrate reaction is stopped and the optical density is read with a micro-well spectrophotometer.

## Intended Use of New Device:

ImmunoWELL EA(D) IgG Test is an ELISA method for the qualitative detection of IgG antibody to Epstein-Barr Virus Early Antigen (Diffuse) in human serum. When used in conjunction with other EBV serologies, results are used to determine immunological response to EBV infection and may aid in determining the stage of convalescent Epstein-Barr virus (EBV) infection.

Technological characteristics of the new device compared to the predicate device: These two devices are essentially the same. Both use a recombinant antigen in a microtiter format. The only noted differences are specific reagent lots (e.g., antigen or conjugate) and selection of the cutoff.

## Performance Characteristics

Two hundred sera submitted for EBV serological testing, including anti-EA-D testing, were evaluated in two laboratories. Site A and GenBio also tested all samples using ImmunoWELL VCA IgG, VCA IgM and EBNA IgG. GenBio also tested the samples using ImmunoDOT Mono G and Mono M test kits. ImmunoDOT detects VCA IgG, VCA IgM and EBNA IgG, but also detects heterophile antibodies using a purified bovine red cell extraction.

EBV diagnostic profile interpretation was made following criteria listed in Table 1. If the profiles determined at GenBio and Site A agreed, it was directly assigned. Initially there were twelve (6%) discrepant profile results. In all discrepant cases, the ImmunoDOT profile result did agree with one site's interpretation, resolving the discrepancy. The EBV serological profile distribution is shown in Table 2.

**Table 1: Profile Interpretation Criteria**

| | VCA IgM | VCA IgG | EBNA IgG |
|---|---|---|---|
| Current or Acute Infection | Positive | Positive | Negative |
| Current, Late or Recent | Positive | Positive | Positive |
| No Past Infection or Negative | Negative | Negative | Negative |
| Past Infection | Negative | Positive | Positive |

**Table 2: EBV Serological Profile Distribution of the Population**

| Profile | Number | Percentage |
|---|---|---|
| Current (Acute) Infection | 17 | 8.5% |
| Current, Late (Recent) Infection | 2 | 1.0% |
| No Past Infection or Negative | 31 | 15.5% |
| Past Infection | 150 | 75% |

It is generally recognized that anti-EA occurs does not occur in subjects with no past infection. This information can be summarized by the following rules:

1. Patients form anti- EA-D during acute, primary infection.
2. Anti-EA-D presence in subjects with past infections (anti-VCA IgG positive, EBNA IgG positive, VCA IgM negative, and heterophile negative) indicates recurrent infection
3. Anti-EA-D should not occur in seronegative subjects.

Based on these criteria, samples from current or acute infected subjects are expected to be anti-EA-D positive, material from people with current-late (recent ) infection is expected to be anti-EA-D negative, sera from subjects with no past Infection should be anti-EA-D negative, and those with past EBV infection and no recurrent infectivity are anti-EA-D negative. ImmunoWELL EA-D performance data, using these criteria, is summarized in Tables 3 and 4. For comparison, the performance characteristics for these same 200 sera using another commerically available anti-EA-D microtiter test kit are shown in Table 5. In all cases, equivocal results are excluded from calculations.

Table 3: Site A Performance Characteristics

| Characteristics | Percentage | Range† |
|---|---|---|
| Relative Sensitivity | 31 (5/16) | 11-59% |
| Relative Specificity (Seronegative, No Past Infection Profile) | 100 (31/31) | 89-100% |
| Relative Specificity (Seropositive, Past Infection Profile) | 92 (133/144) | 87-96% |

† 95% Confidence Interval, based on exact method

**Table 4: Site B Performance Characteristics**

| Characteristics | Percentage | Range† |
|---|---|---|
| Relative Sensitivity | 43 (6/14) | 18-71% |
| Relative Specificity (Seronegative, No Past Infection Profile) | 100 (31/31) | 89-100% |
| Relative Specificity (Seropositive, Past Infection Profile) | 85 (114/134) | 78-91% |

† 95% Confidence Interval, based on exact method

**Table 5: Predicate Device Performance Characteristics**

| Characteristics | Percentage | Range† |
|---|---|---|
| Relative Sensitivity | 44 (7/16) | 20-70% |
| Relative Specificity (Seronegative, No Past Infection Profile) | 87 (26/31) | 69-96% |
| Relative Specificity (Seropositive, Past Infection Profile) | 72 (97/134) | 64-80% |

† 95% Confidence Interval, based on exact method

Note: Please be advised that "relative" refers to the comparison of this assay's results to that of a similar assay. There was not an attempt to correlate the assay's results with the disease presence or absence. No judgment can be made on the comparison assay's accuracy to predict disease.

## Cross-reactivity Study

Three sera each (total of 12 sera) containing high IgG concentrations of anti-varicella zoster, anti-cytomegalovirus, anti-herpes simplex type 1 and anti-herpes simplex type 2 were tested in the assay. All were anti-EA-D negative. In addition, several possible interfering substances (hemoglobin, bilirubin, triglycerides, or cholesterol) were tested by adding a measured amount of the substance into a negative serum and testing for analyte using the ImmunoWELL kit. The interfering substance low level equals the amount normally found in blood serum. The mid level is twice the normal concentration and the high level is four times the amount normally seen in serum. Six negative sera were evaluated. No interference was observed.

## Precision Study

The precision study was conducted at three sites: Site A, Site B and at GenBio. Seven samples were tested. Samples were aliquoted so that each site received three sets of twenty-one samples. The twenty-one samples represented triplicates. The sites performed the test three times. These results are summarized in Table 6.

**Table 6: Assay Precision**

| | Within Run | | Between Runs within Laboratory | | Between Laboratories | |
|---|---|---|---|---|---|---|
| Average (Units/mL) | Standard Deviation (Units/mL) | %CV | Standard Deviation (Units /mL) | %CV | Standard Deviation (Units/mL) | %CV |
| 65 | 5 | 7% | 3 | 4% | 19 | 28% |
| 61 | 5 | 8% | 4 | 6% | 17 | 28% |
| 194 | 10 | 5% | 10 | 5% | 29 | 15% |
| 257 | 18 | 7% | 15 | 6% | 32 | 12% |
| 837 | 78 | 9% | 86 | 10% | 189 | 23% |
| 1211 | 188 | 16% | 181 | 15% | 329 | 27% |
| 1908 | 176 | 9% | 141 | 7% | 380 | 20% |

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 11 2001

Bryan Kiehl, Ph.D.
Vice President
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15222-A Avenue of Science
San Diego, CA 92128

Re: 510(K) Number: K010301
Trade/Device Name: ImmunoWELL® EA(D) IgG Test
Regulation Number: 866.3235
Regulatory Class: I
Product Code: LSE
Dated: April 6, 2001
Received: April 10, 2001

Dear Dr. Kiehl:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

FDA Document Number:

# Indications for Use

**510(k) Number (if known):** K010301

**Device Name:** ImmunoWELL® EA(D) IgG Test

**Indications for Use:**

ImmunoWELL EA(D) IgG Test is an ELISA method for the qualitative detection of IgG antibody to Epstein-Barr Virus Early Antigen (Diffuse) in human serum. When used in conjunction with other EBV serologies, results are used to determine immunological response to EBV infection and may aid in determining the stage of convalescent Epstein-Barr virus (EBV) infection.

Antibody titers to specific EBV antigens correlate with different stages of infectious mononucleosis. Antibodies to EA may appear transiently for up to three months or longer during the acute phase of IM. Antibodies to EA together with antibodies to EBNA and high titers of IgG to VCA may be associated with reactivation of the latent viral carrier state.

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Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K010301

PRESCRIPTION USE X